REMARKS

Claims 47-62 were pending in the above-identified application prior to entry of this Amendment.

The Examiner has objected to the lack of a generic description for conditions 6, 14, 18, 29, 33 and 38 of HAMPTON CRYSTAL SCREEN I and 6, 14, 18, 29, 34, and 36 of WIZARD SCREEN I. Applicants respectfully note that the specific conditions of these screens are found in the catalogs and on-line catalogs and on the websites for Hampton Research and Emerald Biostructures, Inc. both of which are identified in the application in a sufficient manner for one of skill in the art to understand and find the specific conditions set forth in these reagent kits designed for rapid screening for the crystallization of macromolecules. Applicants do not have to identify each component of these kits if they are identified in a sufficient manner to allow one of skill in the art to identify the components with ease. Applicants therefore, respectfully request that the Examiner reconsider and withdraw his objection.

The Examiner has objected to Figure 6a-6d as incomprehensible. Applicants respectfully submit that the drawings submitted to the patent office were prepared by a competent patent draftsperson. This figure can be read in the PCT publication WO 01/77309 which is identical to the instant application. The drawings submitted in the instant application are identical to those submitted in the PCT application. Applicants submit herewith the first page and sheet 5 of the drawings from the PCT application as Exhibit A. Applicants respectfully request that the examiner recheck the formal drawing submitted in this case to ascertain whether the scanning or copying thereof has made Figure 6a-6d incomprehensible.

The Examiner alleges that the specification contains reference to specific amino acid residues not identified by a sequence identification number and that S. aureus is not identified by a sequence identification number at each mentioning of the protein. Applicants have reviewed the application and have amended the specification to insert sequence identification numbers where absent..

The Examiner has also requested that a sequence identification number. be inserted in claims 48, 52, 53 and 54. Applicants have amended claims 47, 48, 52, 53, 54, 55 and 59 to insert

the sequence identification numbers . Applicants therefore respectfully request that the rejection be withdrawn. .

Rejection Under 35 U.S.C. §112, First Paragraph

The examiner has rejected claims 55-62 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and alleged that claims 55-62 include new matter. Specifically, the Examiner alleged that the starting and ending points of the polypeptides recited in claims 55 and 59 are not supported by the originally filed specification. Applicants respectfully traverse the rejection. Independent claims 55 and 59 are each directed to a polypeptide consisting of a portion of S. aureus thioredoxin reductase (SEQ ID NO: 1) that includes the FAD binding pocket. See, for example, Trilateral Project WM4 on Comparative study on "protein 3-dimensional (3-0) structure related claims," Annex 3, Case 5, [Claim 21 (http://www.uspto.gov/web/tws/wm4/pdf/wm4 3d annex 3.pdf).

Independent claim 55 (as amended) recites a polypeptide consisting of a portion of S. aureus thioredoxin reductase (SEQ ID NO: 1), wherein the portion consists of a contiguous stretch of amino acids starting at one of amino acids 10 to 12 and ending at one of amino acids 290 to 297 of SEQ ID NO: 1; and that claim 59 (as amended) recites a polypeptide consisting of a portion of S. aureus thioredoxin reductase (SEQ ID NO: 1), wherein the portion consists of a contiguous stretch of amino acids starting at one of amino acids 43 to 52 and ending at one of amino acids 286 to 289 of SEQ ID NO: 1. Applicants respectfully submit that the claimed polypeptides are adequately supported by the originally filed specification. Specifically, claim 55 is directed to fragments of S. aureus thioredoxin reductase (SEQ ID NO: 1) that include amino acid residues in the FAD binding pocket as listed, for example, in Tables 2-4.

Thus the polypeptide recited in claims 55-58 includes the FAD binding site recited in originally filed claims 1-3. The end points of the polypeptide recited in claim 59 are supported, for example, by the first and last residues listed in Tables 5 to 7 at page 8 of the specification. Thus the polypeptide recited in claims 59-62 includes the NADPH binding site recited in originally filed claims 4-6.

Reconsideration and withdrawal of the rejections are respectfully requested.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 47-54 stand rejected under 35 U.S.C. §112, first paragraph. The Examiner has rejected claims 47-54 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant respectfully traverses the rejection of claims 47-54.

> "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention." M.P.E.P. §2163. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical andlor chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

Claim 47 (as amended) is directed to a method for crystallizing S. *aureus* thioredoxin reductase; and claims 48-54 (as amended) are directed to crystals of S. *aureus* thioredoxin reductase. Applicant respectfully submits that the specification (including, for example, the originally filed claims) provides an adequate written description for methods for crystallizing S. *aureus* thioredoxin reductase. For example, method claim 47 (as amended) recites that the amino acid sequence of the *S. aureus* thioredoxin reductase comprises SEQ ID NO: 1 (e.g., Figures 11 and 15), or SEQ ID NO: 1, except that at least one methionine is replaced with selenomethionine (e-g., page 38, line 27 to page 41, line 2; page 41, line 15 to page 44, line 9; and page 45, lines 8-3 1). Method claim 47 (as amended) further recites appropriate crystallization conditions including, for example, concentration of the *S. aureus* thioredoxin reductase (e.g., page 2, lines 24-25) and solution description: e-g., pH of about 6 to about 10 (e.g., page 13, line 4); about 100 mM to about 6 M sodium formate (e.g., page 13, line 5); and optionally up to about 40 wt. % DMSO (e.g., page 13, line 6). Thus, Applicant respectfully submits that the specification, which

includes the originally filed claims, adequately supports a method for crystallizing *S. aureus* thioredoxin reductase (e.g., claim 47).

Further, Applicant respectfully submits that the specification (including, for example, the originally filed claims) provides an adequate written description for crystals of S. *aureus* thioredoxin reductase (e.g., claims 48-53, as amended). The crystal claims recite various parameters including, for example, space group symmetry (e.g., claim 49; and page 12, line 27), unit cell dimensions (e.g., claim 50; and page 12, lines 28-30), structure coordinates (e.g., claim 51; structure coordinates in Table 1; and description of structure at page 14, line 15 to page 19, line 2), and amino acid sequence (e.g., claims 52-53, as amended; Figures 11 and 15; page 38, line 27 to page 41, line 2; page 41, line 15 to page 44, line 9; and page 45, lines 8-31). Thus, Applicant respectfully submits that the specification adequately supports crystals of *S. aureus* thioredoxin reductase (e-g., claims 48-53, as amended).

Moreover, Trilateral Project WM3 on *Comparative study on "protein 3-dimensional (3-D) structure related claims.* in referring to a hypothetical claim (i.e., "A crystalline form of protein P having unit cell dimensions of a=4.0nm, b=7.8nm, and c=11.0nm") stated that "[the claim complies with the written description requirement because the structure of protein P is provided." Trilateral Project WM4 on *Conzparative study on "protein* 3-*dimensional* (3-D) *structure related claims,* Annex *3,* Case 4, A3 (previously cited). Applicant respectfully submits that the present specification provides the structure of *S. aureus* thioredoxin reductase. *See, for example,* the atomic structure coordinates listed in Table 1, and described, for example, at page *5,* lines 5-16 of the specification.

Based on the remarks presented herein above, Applicant respectfully submits that the specification recites structural, physical, and chemical properties, along with a method of making the claimed invention, sufficient to satisfy the written description requirement under 35 U.S.C. $1 12, first paragraph.

In view of these amendments and remarks, withdrawal of the rejections under 35 U.S.C. §112, first paragraph, is respectfully requested.

ENABLEMENT

The Examiner rejected claims 1-7 and 47-53 under 35 U.S.C. *3* 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention..

"A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." M.P.E.P. §2164.04. "As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. §112 is satisfied." M.P.E.P. §2164.01(b). "For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the *art* could not *use* the genus as a whole without undue experimentation." M.P.E.P. §2164.02, paragraph entitled "WORKING EXAMPLES AND A CLAIMED GENUS" (emphasis added). "[Even in unpredictable arts, a disclosure of every operable species is not required." M.P.E.P. §2164.03.

Applicant further submits that claims 47-54 are fully enabled by the specification. Although not required, the specification includes working examples of methods for crystallizing *S. aureus* thioredoxin reductase (e.g., page 41, lines 4-18; and page 44, line 11 to page 45, line 6). The specification also provides methods of using the claimed crystals (e.g., homology modeling and rational drug design; page 29, line 23 to page 36, line 29). Moreover, the Examiner has not provided any reason to doubt the objective truth of the disclosure provided in the specification. Moreover, Applicant respectfully submits that one of skill in the art, using the disclosure provided in the specification (including the working examples), would be able to make and use

the entire scope of the invention as recited in claims 47-53. For example, Applicant's Representatives respectfully submit that the present disclosure of methods of making and using crystals of S. *aureus* thioredoxin reductase provides enablement for one of skill in the art, without undue experimentation, to make additional crystals of S. *aureus* thioredoxin reductase. For example, Applicant's Representatives respectfully submit that the presently disclosed crystals provide enablement for one of skill in the art to use the crystals in, for example, cross-seeding techniques to make additional crystals of S. *aureus* thioredoxin reductase. Thus, Applicant respectfully submits that claims 47-53 (as amended) are fully enabled by the specification. Based on the remarks presented herein above, Applicant respectfully requests that the Examiner reconsider and withdraw the rejections under 35 U.S.C. §112, first paragraph.

The above discussion and corresponding Amendments are based on section 112 issues and are not made to overcome art-based rejections. Accordingly, such discussion and corresponding Amendments should not be construed in a limiting manner.

Applicants attorney attempted to telephone the examiner to discuss the claim amendments however, the examiner was on vacation and unavailable. Applicants' attorney invites the examiner to call the undersigned discuss any remaining issues when he returns from vacation.

It is respectfully submitted that the claims have been put in condition for allowance. Notification to this affect is earnestly solicited. The Examiner is encouraged to contact the Applicants' undersigned attorney to discuss this matter if any questions should arise upon further examination of the pending claims.

Respectfully submitted,

August 25, 2005
Date

Rosanne Goodman
Reg. No. 32,534
734-622-4182